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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 09/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,186	KERKMANN-TUCEK, AIDA	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-5, 7, 8 and 11-13 have been amended. Claim 6 has been canceled. Claims 1-5 and 7-13 are pending and under consideration.

2. Text of sections of Title 35, U.S.Code not foundin this action can be found in a prior action.

3. Claims 11 and 13 are objected to because of the following informalities:
(i)the article "A" is missing before the phrase "Tumor cell library" in claim 11.
(ii) Claim 13 recites "of the tumor cell library" rather than "or the tumor cell library".
. Appropriate correction is required.

4. Claim 13 is rejected under 35 U.S.C. ' 101 because the claim is not presented in the format of a proper process claim. See MPEP 2173.05(q).

5. The rejection of claims 1-5 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter as the claims can read on cells that exist within mammals is maintained for reasons of record. Claims 7 and 8 are also rejected for the same reasons of record. Applicant contends that the claimed subject matter is not directed to cells that naturally exist within the body. this has been considered but not found persuasive. When given the broadest reasonable interpretation, the claims read on tumor cells ex vivo and in vitro. Further, claim 1 has been amended to incorporate the subject matter of Table 1 entitled "Frequent HLA combinations". It appears that the tumor cells claimed do exist as cells which naturally occur within the human body. Amendment of the claims to recite "isolated tumor cells" would overcome this rejection.

6. Claims 1-5, and 7-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A) The metes and bounds of claims 1 and 9 cannot be determined. Claims 1 and 9 recite "a combination of MHC I and MHC II genes, occurring in humans". It is unclear if the limitation of "occurring in humans is to be applied to the origin of the MHC genes, or the origin of the tumor cells, or if "occurring in humans" refers to an analogous occurrence in humans, such as the mouse genes encoding MHC I and II correspond to the HLA genes of humans. for purpose of examination, all alternative will be considered.

(B) It is unclear how the first active method step of claim 9, "tissue typing of tumor cells" relates to the method objective or producing tumor cells according to claim 1, or to the subsequent active method steps in claim 9. It is further unclear how the active method step (c), which requires the selection for tumor cells which express both the MHC I and MHC II genes, can be applied to the product resulting from the active method step of (b) which allows for the transfection of either MHC I or MHC II genes. Further, the metes and bounds of what constitutes "tissue typing" is not defined and can read on the simple determination of the presence or absence of MHC I and MHC II or it can read on the identification of the specific histocompatibility genes present in the same (i.e. HLA-2.1).

(C)Claim 7 is vague and indefinite because it is unclear if the combination entails one MHC I gene and one MHC II gene, wherein the MHC I genes and the MHC II genes are referred to in the alternative, or if the combination is a tumor cells which must collectively comprise all the recited genes. For purpose of examination, all alternatives will be considered.

(D)Claim 8 is vague and indefinite in the recitation of combination of "MHC I/II genes". It is unclear if "MHC I/II" means MHC I or MHC II or MHC I and MHC II. Further it is unclear if the combination must include all of IFN-gamma, CD44 and GM-CSF or if these proteins are referred to in the alternative. It is also unclear how the listing which begins with A*0101; Cw*0701, etc limits the subject matter of the combination of "MHCI/II" because it is unclear if these alleles are to be as a collective combination, or if these alleles are referred to in the alternative.

(E) Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 13 is drawn to the "use of the tumor cells according to claim 1, or the tumor cell library according to claim 11 or the vaccines according to claim 12" are vague and

indefinite. The claims are drawn to a method of using tumor cells, vaccines and tumor cell libraries, but fail to set forth any active, positive steps that define the claimed method.
(F) Claims 11 and 12 are vague and indefinite in the recitation of "comprising the tumor cells according to claim 1". It is unclear if "according to claim 1" requires all of the tumor cells in the table, or if claim 1 requires only a single gene from the table or if "according to claim 1" requires the duplication of a naturally occurring set of genes, such as those exemplified by the Cornish.
(G) It is unclear how the phrase "conventional auxiliary agents" in claim 12 further modifies the term "tumor cells according to claim 1" for purpose of examination, the claim will be read as "according to claim 1 and conventional auxiliary agents".
(H) Claim 9 is vague and indefinite because step c requires the selection for tumor cells with MHC I and MHC II genes, however, step b only requires the transfrection of tumor cells with MHC I or MHC II.

7. Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention..

Claim 12 is drawn to vaccines comprising the tumor cells according to claim 1 and conventional auxiliary agents. Claim 13 is drawn to "use of the tumor cells, tumor cell library or vaccines for the prophylaxis and/or treatment of temporal diseases.

The specification does not provide guidance for how to make a vaccine preparation based on said tumor cells or tumor cell libraries. The term vaccine is defined by the art (Stedman's Medical Dictionary, 27th Edition, 2000, definition for "vaccine") as a prophylactic immunotherapeutic composition. Thus, the claimed vaccine would have to be able to prevent the growth of tumors in a patient and the specification provides no guidance as to selecting patients at risk for developing a specific type of tumor, and the time at which to begin administering said vaccine..

In the event that applicant amends the claims to "pharmaceutical composition" rather than "vaccine" and deletes reference to "prophylaxis" the specification is still not enabling for how to make and use such a composition with respect to the treatment of tumoral diseases.

Immunotherapy of cancer by the administration of vaccines comprising tumor antigens is highly unreliable. The prior art teaches that tumor cells are phenotypically less stable than normal cells and can escape the immune response of the host by many mechanisms including deficient antigen processing by tumor cells, production of inhibitory substances such as cytokines, tolerance induction, rapidly growing cells which can overwhelm a slower immune response, failure of the host to respond to an antigen due to immunosuppression, tumor burden, infections or age, deficient antigen presentation with the host and failure of the host effector cells to reach the tumor due to the stromal barrier (Paul, Fundamental Immunology, (text), 1993, page 1163, second column, first sentence under the heading "Factors Limiting Effective Tumor Immunity" and Table 4). The specification has provided evidence that two T-cell clones are able to lyse tumor cells expressing an epitope of the claimed tumor rejection antigen precursors in vitro. Paul teaches that lymphocytes from tumor bearing patients have frequently been found to be cytotoxic to their own tumor cells in vitro, but that this effect was blocked by the addition of sera from said patients. Paul teaches that the constituent of the sera which caused the blocking of the cytotoxicity was unknown, but that antibodies, antibody-antigen complexes and shed antigen have all been implicated in the blocking phenomenon (Paul page 1167, second paragraph under the heading "Immunological Enhancement and Blocking Factors"). Paul also notes that in some cases, immune response to a tumor antigen may sometimes stimulate the growth of the tumor cells directly (last line under the heading "Immunological Enhancement and Blocking Factors", page 1167). With respect to the blocking factor found in serum, Apostolopoulos et al (Nature Medicine, 1998, vol. 4, pp. 315-320) teach that endogenous antibodies present at the time of administration of a tumor peptide re-routes the immune response from a cellular response to a humoral response. In preclinical experiments with mice, MUC1 peptides targeted to the mannose receptor produce high levels of CTL and a low level of antibodies. However, in human clinical trials a low level of CTL and a high level of humoral response was observed (Apostolopoulos, page 315, first column, bridging paragraph). Apostolopoulos et al teach that the presence of endogenous antibodies which bind to the MUC1 peptide was responsible for this re-routing of the immune response from cellular to humoral due to the Fc portion of the antibody (page 319, first column, lines 7-10). Apostolopoulos et al teach that mice are devoid of these antibodies (page 315, second column, lines 9-13) and are thus able to effectively mount a cellular

immune response against the target antigen. Apostolopoulos et al teach that these findings have implication for other immunotherapy approaches (page 318, lines 4-8, under the heading "Discussion".. In support of these conclusions Jager et al (PNAS, 2000, Vol. 97, pp. 12198-12203) teach that patients who do not have antibodies to the cancer testis antigen, NY-ESO-1, were able to generate a specific T-cell response to NY-ESO after intradermal administration, whereas patients having antibodies prior to treatment which reacted with said antigen already had T-cells which reacted with target cells expressing said antigen in vitro, and said positive patients did not develop significant CTL in response to the administered NY-ESO antigen. These references serve to demonstrate that the induction of a anti-tumor CTL response after the administration of a tumor peptide is unpredictable.

Paul (ibid) states that deficient antigen presentation is a mechanism by which tumor cells escape immune detection. This is corroborated by the observations set forth in the abstract of Semino et al (Journal of Biological Regulators and Homeostatic Agents, 1993, Vol. 7, pp. 99-105) and the abstract of Algarra et al International Journal of Clinical and Laboratory Research, 1997, Vol. 27, pp. 95-102) which all teach that primary tumors in situ are often heterogeneous with respect to MHC presentation. The effect of the claimed vaccine upon such a heterogeneous tumor has not been demonstrated by the specification. More currently, Bodey et al (Anticancer Research, 2000 Jul-Aug, Vol. 20, pp. 2665-2676) teach that the failure of methods of treating cancer comprising the administration of tumor antigens is due to the failure of cancer vaccines to eliminate the most dangerous cells within a tumor which are so de-differentiated that they no longer express cancer cell specific molecules (abstract).

Paul (ibid) states that the induction of tolerance is a mechanism by which tumor cells escape immune detection. The art recognizes that T-cell are subject to clonal deletion within the thymus of a host and that this mechanism eliminates t-cell which are reactive with self-antigens. The specification teaches that the polypeptide encoded by SEQ ID NO:2 is indeed a self antigen, rather than a mutated self antigen, as it is expressed on normal tissues as well as cancerous tissues. Lauritzsen et al (International Journal of Cancer, 1998, Vol. 78, pp. 216-222) teach that clonal deletions of thymocytes is a major event in T-cell tolerance which could lead to a tumor escape mechanism. In transgenic mice homozygous for HLA-specific CD+4 T-cells which are specific for a MOPC315 plasmacytoma, injection of a large number of tumor cells results in

apoptosis of immature and mature transgenic CD+4+8 and CD+4 thymocytes. This negative selection was specific for the transgenic thymocytes that would complement the idiotype of the immunoglobulins of the MOPC315 plasmacytoma, because injection of tumor cells from a plasmacytoma which had a different idiotype of immunoglobulins failed to elicit the clonal deletion. Lauritzsen et al teach that injection of purified MOPC315 protein, versus the tumor cells, caused a profound reduction of the specific thymocytes specific to the idiotype of the plasmacytoma. Lauritzsen et al conclude that deletion of tumor specific thymocytes may represent a major escape mechanism in patients with cancers that secrete of shed antigens. In the instant case, the antigens are known self antigens. It would be reasonable to conclude that said normal antigens are presented within the thymus to developing thymocytes and T-cells with high affinity for said antigens are deleted as "self". It would be also reasonable to conclude that administration of the claimed polypeptides or cells expressing said polypeptides would not result in an efficacious vaccine as a T-cell response would not be evoked due to the process of clonal deletion in the thymus, rendering the host devoid of T-cells which are specific to the self-protein. Sarma et al (Journal of Experimental Medicine, 1999, Vol. 189, pp. 811-820) states that a critical issue in therapeutic regiments comprising the administration of tumor antigens for immunotherapy is whether unmutated tumor antigens which are expressed in normal cells impose special restrictions on the CTL response in vivo. Using transgenic mice wherein the antigen specific T cells specific for the P1A non-mutated tumor antigen are expressed at high levels and remain responsive to the P1A antigen when assayed in vitro, it was found that P1A antigen expressed in the thymus resulted in clonal deletion of said specific T-cells Sarma et al note that although said transgenic mice produce an overwhelming majority of T cells that are specific for P1A, said mice are no more resistant to cells expressing P1A than non-transgenic litter mates. Sarma et al concludes that even thought P1A can be a tumor rejection antigen, the effector function of P1A specific CTL is restrained in vivo and that these results have important implications for the strategy of tumor immunotherapy. With regard to the isolation of two T-cells which are specific for the instant antigen presented in the context of HLA-A24, it cannot be determined if this is a reliable indicator that in all patients, with any of the types of cancers listed on page 20, would have a T-cell available after thymic selection which would react with said antigen in the context of HLA-A24 or any other MHC molecule. Further, the presence of CTL

which can lyse target cells in vitro has no apparent nexus with anti-tumor cytolytic activity in vivo. Ohlen et al (Journal of Immunology, 2001, Vol.166, pp. 2863-2870) teach that T-cells recognizing normal proteins expressed in tumors can be isolated in vitro, but that the existence of said T-cells does not preclude in vivo anergy induction and deletion (page 2863, second column, lines 1-6 of the last paragraph). Antoinia et al (International Immunology, 1995, Vol. 7, pp. 715-725) teach that T-cells which are impaired in the ability to proliferate in response to antigen and unable to reject tumors in vivo were fully functional as CTL lymphocytes in vivo (page 724, first column, first full paragraph). These references serve to demonstrate that the lysis of target cells expressing tumor antigens in vitro does not constitute evidence that said T-lymphocytes would be effective at lysing tumor cells in vivo.

Thus, it appears that the interaction of the tumor cells with the host can produce tolerance by means of clonal deletion within the thymus of said host. Furthermore, the relationships between the multitude of different tumor cells would be variable as different types of organs (neuroblastoma, brain, colorectal, gastric, head-and neck, lung, prostate, breast, thyroid, bladder, kidney, leukemia, etc) and different histological types of neoplasms (carcinoma, squamous cell, mesothelial, neuroepithelial, sarcoma, leukemia, etc) all present tumor antigens.
It is concluded based on the references discussed above, that the state of the art with respect to treating patients with cancer by means of administering a vaccine made form tumor antigens is unpredictable. The specification does not provide any specific guidance on how to make such a vaccine. The specification does not provide any disclosure that the administration of tumor antigens taken from cells as indicated in claim 1would generate CTLs which lyse the cells of a tumor in situ,. Thus, without a demonstration that the administration of the a vaccine derived from the cells propagated by the claimed method which would overcome immunosuppression of the host, the rapid growth of the target tumor cells, as well as overcoming the stromal barrier and tolerance induction in the host and objective evidence that the target tumor cells in vivo present adequate tumor rejection antigen on the surface of all the tumor cells, one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to make and use the vaccine and tumor cell library of claims 12 and 13.

8. Claims 1-5 and 7-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Lindauer et al (Immunology, March 1998, vol. 93, pp. 390-397, cited in the previous action) as evidenced by the abstract of Lahm et al (Cancer Research, 1994, Vol. 54, pp. 3700-3702). Claim 3 embodies the method of claim 2 wherein the co-stimulatory molecules comprise either B7 or CD44. Claim 4 embodies the tumor cells of claim 1 wherein one or several genes code for cytokines and wherein the one or several genes are expressed. Claim 5 embodies the tumor cells of claim 4 wherein the cytokines are interleukins, GM-CSF, TNF-alpha or IFN-gamma. Claims 7 and 8 embodies the tumor cells according to claim 1 comprising a combination of MHC I and MHC II genes and a combination of MHC/MHCII genes and genes for IFN-gamma, CD44 and GM-CSF, and a list of alleles, respectively. . It is noted that the metes and bounds of claim 7 cannot be determined for the reasons set forth in the rejection under 112, second paragraph, above. Claim 9 is drawn to a method for producing the tumor cells according to claim 1 comprising tissue typing of the tumor cells, transfection of the tumor cells with MHC I/MHC II and selection for tumor cells which express the MHC I and MHC II genes. Claim 10 embodies the method of claim 9 wherein the tumor cells are further transfected with one or several genes coding for co-stimulatory molecules and/or cytokines and selected for the expression of these genes.

Lindauer et al disclose the human colorectal tumor cell, SW480 (page 391, first column, under the heading "Cells"), transfected with HLA-DR (MHC II) and B7 (CD80/CD86) (page 393, second column, lines 9-17, under the heading "Class II MHC expression in combination with CD54 and CD80 directly induces T-cell proliferation") thus fulfilling the limitation of claims 2, 3 and 10 drawn to the expression of co-stimulatory molecules and specifically B7. The transfected tumor cells also expressed MHC I (page 393 second column to page 394, first column, bridging sentence). Lindauer et al determined that the SW480 cells lack surface class II expression before the transfection (page 393, second column, lines 1-2 under the heading "Class II MHC expression in combination with CD54 and CD80 directly induces T-cell proliferation"), thus fulfilling the specific embodiment of claim 9 drawn to tissue typing. The abstract of Lahm et al provides evidence that the SW480 cells naturally secrete GM-CSF, thus fulfilling the specific embodiments of claims 4, 5 and 8 which specify that the tumor cells express genes which code for GM-CSF. Lindauer et al do not specifically state the specific allele of HLA-

DR3 used in the experiment, however, it appears that it could have been one of the HLA-DR alleles listed in claim 1. Further, all cells express MHC class I, therefore the SW480 cells would inherently express on the alleles listed under HLA-A, HLA-C or HLA-B. Thus the claimed tumor cells appear to be the same as the prior art tumor cells, absent a showing of unobvious differences. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the tumor cells of the prior art do not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

9. Claims 1-3, 7-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Dessureault et al (Journal of Surgical Research, 1996, Vol. 64, pp. 42-48, cited in the previous action).

Dessureault et al teach human melanoma cells transfected with the B7.1 co-stimulatory molecule. Dessureault et al teach that said melanoma cells express both MHC I and MHC II (abstract, lines 3-7 and lines 11-15).

Dessureault et al do not specifically state the specific allele of MHC II used in the experiment, however, it appears that it could have been one of the HLA-DR, DQ or DP alleles listed in claim 1. Further, the melanoma cells were confirmed to express MHC I. Thus said melanoma cells would inherently express on the alleles listed under HLA-A, HLA-C or HLA-B. Thus the claimed tumor cells appear to be the same as the prior art tumor cells, absent a showing of unobvious differences. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the tumor cells of the prior art do not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

10. Claims 1, 7, 8 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by van Duinen et al (Cancer Research, 1988, Vol. 48, pp. 1019-1025). VanDuinen et al disclose a panel of tumor cells in Table 2, which fulfill the specific embodiment of claim 1 because said panel comprising tumor cells having both HLA class I antigens and HLA class II antigens. Van Duinen et al do not specifically disclose the specific allele of MHC II detected in the melanoma cells, however, it appears that it could have been one of the HLA-class I and HLA class II alleles listed in claim 1. Thus the claimed tumor cells appear to be the same as the prior art melanoma cells, absent a showing of unobvious differences. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the tumor cells of the prior art do not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

11. Claims 1, 2, 7, 8 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Moller et al (International Journal of Cancer, Supplement, 1991, Vol. 6, pp. 155-162) as evidenced by Abbas et al (Cellular and Molecular Immunology, 1991, page 152) Moller et al disclose a panel of 149 colorectal carcinomas in Table 1, which fulfill the specific embodiment of claim 1 because said panel comprising tumor cells having both HLA class I antigens and HLA class II antigens. Moller et al further disclose that said tumor cells also expressed high levels of LFA-3 which fulfills the specific embodiment of claim 2 specifying the expression of one or several genes which code for co-stimulatory molecules as evidence by Abbas et al who disclose that LFA-3 is an accessory molecule on the target which lead to increases in adhestion between a T-cell and a target cell. Moller et al do not specifically disclose the specific allele of MHC II detected in the colorectal tumor cells, however, it appears that it could have been one of the HLA-class I and HLA class II alleles listed in claim 1. Thus the claimed tumor cells appear to be the same as the prior art tumor cells, absent a showing of unobvious differences. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the tumor cells of the prior art do not possess the same material, structural and

functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

12. All other rejections and objections as set forth in the previous Office action are withdrawn in light of applicants amendments.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
9/7/2004

Karen A. Canella
KAREN A. CANELLA PH.D
PRIMARY EXAMINER